A CONTRIBUTION TO THE STATISTICS ON THE PRESENCE OF DIPHTHERIA BACILLI IN APPARENTLY NORMAL THROATS

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A CONTRIBUTION TO THE STATISTICS ON THE PRESENCE OF DIPHTHERIA BACILLI IN APPARENTLY NORMAL THROATS.*

REPORT OF 1,000 CASES EXAMINED (1905–6).

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ALMOST since the discovery of the diphtheria or Klebs-Löffler bacillus, the presence of these organisms or morphologically similar organisms in the throats and noses of persons showing no clinical evidence of diphtheria has been recognized and numerous investigations to determine their mode of entrance, their frequency, their meaning, and virulence, etc., have been made.

According to R. O. Neumann, virulent diphtheria bacilli are **never** found in **normal** throats and noses, but in those cases where catarrhal conditions are present. Of some 206 people examined by him, of whom 111 were normal and 95 were suffering from nasal troubles, none with normal mucous membranes harbored virulent diphtheria bacilli, whereas 8 per cent of those suffering from acute and chronic catarrhs showed true virulent diphtheria bacilli. Pseudodiphtheria bacilli, under which he includes both *B. xerosis* and Hoffman's bacillus, were isolated from 98 per cent of the normal and 97 per cent of the affected cases, and are considered by him as normal inhabitants. Other observers, chiefly the earlier ones, give on the other hand the impression that the Klebs-Löffler bacillus is fairly common in the mouths of normal persons, and this impression prevails to large extent among physicians, who are inclined to think the condition so common that it can be ignored. Still others show that there is a certain small percentage of cases which harbor diphtheria bacilli where, as far as can be discovered, no recent and direct exposure to or previous infection by diphtheria can be traced. These cases are found, however, rather in cities and in institutions where diphtheria is always present to greater or less extent.

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Steenmeyer investigated a small series of children from a village where no diphtheria had existed for 10 years and compared these with a similar number of children taken from the surgical wards of a hospital in Rotterdam. Of the former, 52.4 per cent showed organisms resembling diphtheria bacilli (pseudodiphtheria probably included?) but none was virulent, whereas, the city children gave a percentage of 75.6 similar organisms and of these 7.3 per cent were virulent. Of the 330 normal non-exposed persons examined by Park and Beebe (1894) in N. Y. City, 9.7 per cent showed organisms morphologically similar to the diphtheria bacilli, but only 2.4 per cent were virulent[1] to animals. One-fourth of those infected with virulent bacilli subsequently came down with diphtheria. Fibiger in Copenhagen (1895) found 11.1 per cent non-virulent diphtheria-like organisms in healthy mouths and 2.9 per cent virulent Klebs-Löffler bacilli. Kober (1899) in Breslau examined 600 school children and found 1.6 per cent harbored non-virulent and 0.83 per cent virulent diphtheria bacilli. In all of these infected children he traced exposure to diphtheria, more or less remote. Denney (1900) out of 235 normal persons, and Graham-Smith, out of 362, found none infected with virulent Klebs-Löffler bacilli; those found were non-virulent. E. Miller (1896) examined a series of 100 children on admission to an institution and found 24 per cent with diphtheria-like bacilli in their throats. Of the 12 tested on animals, 6 were virulent. In only one case of the 24 was there known exposure to diphtheria. Later 18 children in the same institution, who had negative cultures on admission, gave positive cultures after being in the house for some time. Four of these were virulent. There are many other investigators who have found varying percentages of infected throats, Stross, Cobbett, Gross (7.9 per cent), Hewlett and Murray (15 per cent), etc., but on the whole their statistics are not very valuable for our purpose, chiefly because of the incompleteness of their virulence tests.

Recently, January 1907, M. E. Pennington of the Philadelphia Health Bureau has published the results of her investigations among well school children. From 25 schools taken at random, she found 9.3 per cent of the children infected with diphtheria-like organisms. About one-half of these organisms were to a greater or less degree pathogenic to guinea-pigs and 13.5 per cent were highly virulent. Some of these children were exposed to diphtheria.

Unless the conditions are parallel in the different investigations, or unless these are taken into account, it is manifestly unfair to compare statistical results. That virulent diphtheria bacilli are found in normal throats of persons exposed to diphtheria is unquestioned, but how far they are present in normal non-exposed persons is still a mooted point. The results depend largely on what each individual investigator considers as a "normal throat," how far he differentiates the members of the group of organisms showing the morphological characteristics of the diphtheria bacillus, on the environment of the cases examined, and the severity of the disease as it exists in the community. In a city like New York, where there are some 8,000–12,000 cases of diphtheria reported each year and the possible

[1] By virulent we mean producing diphtheria toxin.

sources of infection are so many, tenements, schools, shops, public conveyances, hotels, restaurants, etc., it is almost impossible to trace in every case exposure to the infection. It is certainly most plausible to believe that infection always comes from a previously infected individual, whether it be mediate or direct, remote or recent.

With this in mind the object of the present investigation was not to prove or deny the presence or absence of true diphtheria bacilli in the healthy throats of persons *never* exposed to diphtheria, but simply to determine approximately in what number of the apparently normal throats of individuals among whom diphtheria is most frequent, viz., children in crowded tenements and institutions, virulent diphtheria bacilli are found. Two series of cases were examined, first, those as far as known not recently or directly exposed to diphtheria; second, those directly and definitely exposed in their families.

SERIES I.

The first series of cases examined (1,000 in all) were, with a few exceptions, taken from among the tenement-house children who came for treatment to the dispensaries and hospitals of the city and from the nurseries of the N. Y. Foundling Asylum. As far as possible inquiry into immediate and recent exposure to diphtheria was made and noted, and no child suffering from an angina or anything suggesting a "sore throat," nasal discharge, or laryngitis, was included in the series. There was no routine examination for adenoids, large tonsils, or abnormalities of the nose, but a clean fauces alone was considered "normal."

Of the 18 cases in which virulent Klebs-Löffler bacilli were found there was only one in which a possible history of exposure several weeks before was obtained. In the children from the hospital wards and nurseries, while there was no definite exposure to clinical diphtheria, so-called "laboratory cases" with bloody nasal discharge had been in the wards for short intervals until the clinical symptoms developed. In the Babies' Hospital there were four such nasal cases in the wards for one or two days during March and April, from which virulent diphtheria bacilli were isolated. One of these children also had non-virulent diphtheria bacilli in his throat. This child was considered to have given diphtheria to the nurse who took

care of him (he was isolated as soon as the bacilli were discovered) and to another child. The one "normal" child in the Babies' Hospital from whom virulent organisms were isolated was down on the records as having been exposed to diphtheria and had been given an immunizing dose of antitoxin during a previous admission three months and a half before. He also subsequently developed a bloody nasal discharge from which Klebs-Löffler bacilli were isolated.

In another hospital from which no positive cultures were obtained from any of the normal children, there was in the same ward a child suffering from a post-diphtheric paralysis, from whose throat virulent Klebs-Löffler bacilli were obtained.

With the exception of 50 children, cultures were taken from the throats alone, so that it is very possible the percentage of bacilli found might have been somewhat higher, especially of the pseudo-diphtheria bacilli, if nasal cultures had been made at the same time. Wesbrook, Wilson, and McDaniel (1899) found this true among the children in a boarding-school investigated by them. To determine how far this might be so in our cases, 50 children were examined, cultures being taken from each side of the nose and from the throat (Table 1). In two per cent of the cases virulent Klebs-Löffler bacilli were found in the nose alone. Pseudodiphtheria bacilli were found about twice as often in the nose as in the throat.

TABLE 1.

NOSES VS. THROATS.

Source	Number Examined	Ages	Diphtheria-like Bacilli Isolated from Nose Alone	Diphtheria-like Bacilli Isolated from Throat Alone	Diphtheria-like Bacilli Isolated from Both	Virulent	Non-virulent	*B. Xerosis* from Nose Alone	*B. Pseudodiphtheria* from Total Noses	*B. Pseudodiphtheria* from Total Throats	*B. Pseudodiphtheria* from Both Nose and Throats
Babies' Hospital wards.....	28	2 weeks to 3 yrs.	1	0	0	1	0	0	23	10	10
N. Y. Infirmary dispensary.....	22	2 mos. to 10 yrs.	0	0	1	0	1	1	9	5	3
Total.....	50		1 2%	0	1	1 2%	1	1	32 64%	15 30%	13 26%

The technique was that in general use. Löffler serum tubes were inoculated according to the usual board of health directions and examined the following day, after incubation. From all the tubes

that were positive or suspicious, plates and ascitic broth tubes were inoculated. After isolation of the organisms, with the exception of the pseudodiphtheria or Hoffman's bacillus, all were tested in the usual way on guinea-pigs for virulence. Guinea-pigs weighing from 200 to 300 grms. were inoculated subcutaneously at the outset with 1 c.c. and 0.5 c.c. respectively of 48-hour ascitic broth cultures of the strain tested, each pig being controlled by a similarly inoculated animal receiving in addition a counteracting dose of diphtheria antitoxin. The strains that killed pigs within the four days were again tested in every case with smaller doses (always controlled by antitoxin) up to 0.1 c.c. When the initial injection did not kill, larger doses sometimes up to 10 c.c were given. Table 2 shows the relative toxicity of the 56 strains isolated.

TABLE 2.

VIRULENCE TESTS.

(The doses cited are the minimum that killed and the maximum that did not kill.)

Death of Unprotected Pig Within	Number Receiving 0.1 c.c.	Dose 0.2 c.c.	Number Receiving 0.5 c.c.	1 c.c.	2 c.c.	5 c.c.	10 c.c.
24 hours.....	2			1*			
48 hours.....	3	1	6				
72 hours.....	1		1				
4 days.....			1	1			
3 weeks.....				1			
Non-virulent...				26	3	1	8

*Virulence of this strain is doubtful as 0.5 c.c. from same broth culture did not kill when inoculated subcutaneously into 250 grm. guinea-pig; virulence test was not repeated.

The pigs charted above as killed by 1.c.c., 0.5 c.c., 0.2 c.c., all received smaller doses up to 0.1 c.c., which did not kill.

Where there was any doubt as to the identity of a supposed pseudodiphtheria bacilli, cultural tests and animal inoculations were used to establish it. The organisms were classified as follows: (1) true virulent Klebs-Löffler bacilli; (2) non-virulent diphtheria-like bacilli; (3) xerosis bacilli; (4) pseudodiphtheria or Hoffman bacilli (alkali producing in glucose broth).

From Table 3, it will be seen that in four instances organisms which behaved somewhat differently culturally from the ordinary diphtheria bacillus were isolated. The growth on Löffler serum was very delicate and the colonies sometimes were not visible for 48 hours. They did not produce toxin and were identified as *B. xerosis*. In

10 c.c. doses, in one case the pig controlled by antitoxin died, in another both pigs died, and in the remaining two neither animal died. From one child this organism and a non-virulent diphtheria-like organism were isolated at the same time.

Tables 3, 4, and 5 give the results of the investigations with the number of cases examined, according to season, ages, and source of material respectively.

TABLE 3.

NORMAL THROATS. SEASON.

1905–6	Number of Cases Examined	Virulent Klebs-Löffler Bacilli in	Non-Virulent Diphtheria-like Bacilli in	Total Diphtheria-like Bacilli in	Pseudodiphtheria Bacilli (Hoffman's)	*B. xerosis*
August 30–31, 1905	21	0	0	0	0	
September.....	30	0	1	1	1	
October.....	31	0	0	0	0	
November.....	10	0	0	0	6	
December.....	27	0	4	4	4	
January, 1906.....	69	2	3	5	35	2
February.....	56	1	2	3	20	1
March.....	107	3	3	5	24	
April.....	37	0	0	0	6	
May.....	152	3	6	9	18	
June.....	94	2	7	10	50	1
July.....	169	4	10	14	47	
August.....	190	3	2	5	52	
October.....	7	0	0	0	3	
Total.....	1,000	18 (1.8%)	38 (3.8%)	56 (5.6%)	266 (26.6%)	4 (.4%)

TABLE 4.

NORMAL THROATS. AGE.

Ages	Number Cases Examined	Total Diphtheria-like Bacilli Isolated from	Virulent Klebs-Löffler Bacilli in	Pseudodiphtheria Bacillus (Hoffman's b.) in
Under 1 year.....	183	6	3	50
1–2 years.....	141	7	6	45
2–3 years.....	112	6	4	33
3–4 years.....	131	11	4	35
4–5 years.....	107	8	2	29
5–6 years.....	61	4	2	25
6–12 years.....	184	12	1	46
12–20 years.....	33	0	0	3
20+ years.....	29	1	0	0
Unknown.....	19	1	0	0
Totals.....	1,000	56	18	266

A casual examination of Table 3 would lead one to infer that a larger number of diphtheria-like organisms were isolated in the summer months during the period when diphtheria is least prevalent. This is due not only to the fact that more cases were examined during the latter six months of the investigation, but chiefly because the majority of the children examined, in contrast to the earlier

TABLE 5.

NORMAL THROATS. SOURCE.

Source of Cases	Number of Cases	Diphtheria-like Bacilli found in	Virulent Klebs-Löffler Bacilli Found in
New York Infirmary for Women and Children dispensary	341	24 or 7 %	9 or 2.6 %
New York Babies'Hospital dispensary	216	7 " 3.2	1 " .46
New York Babies'Hospital wards	125	4 " 3.2	1 " .8
New York Foundling (nurseries)	115	14 " 12.1	4 " 3.5
St. Mary's Hospital, surgical and medical wards	44	0	0
Bellevue Hospital, surgical and medical wards	56	3 " 5.2	0
Contagious Disease Hospital, Kingston Ave., Brooklyn, scarlet-fever and measles wards	61	3 " 4.9	2 " 3.2
NewYork Polyclinic dispensary and wards	42	1 " 2.4	1 " 2.4
Total	1,000	56	18

cases, were those in the hospital wards and the nurseries. For example, all of the cases taken during July came from the New York Foundling, Bellevue, the Babies', and St. Mary's Hospitals, likewise the majority of those examined during June and August, whereas previous to March all came from the out-patient clinics.

The children from the Foundling Asylum were all healthy children from the nurseries, playing around in the open air on the roofs almost all day, but sleeping in the same dormitories at night. They averaged from 2 to 5 years of age.

The children at the Babies', St. Mary's, and Kingston Avenue Hospitals were confined to the wards all the time. Some of the surgical cases from Bellevue were out in the open air part of the time. From the Kingston Avenue Hospital only one child from each of the scarlet-fever and measles wards harbored virulent diphtheria bacilli.

In New York City the mortality from diphtheria in the last 13 years has gradually dropped from 36.4 per cent in 1893, to 10.3 per cent in 1905. Whatever this be due to, whether the earlier recognition and treatment of the disease, better isolation, the use of antitoxin, or the natural wave-like variation in the intensity of the disease, we might at the same time expect a corresponding diminution in the number of normal people infected. In comparing our results with those of Park and Beebe (1894) with whose investigation ours is more nearly analogous, we find the decrease not commensurate. However, while the mortality has decreased since then, the average yearly number of persons reported to the Health Department as clinic-

ally infected with diphtheria has remained practically the same, and because of the comparative mildness of the disease, the number of unrecognized anginal cases and those simulating tonsilitis probably contribute to the spreading of the infection.

SERIES 2.

The second series of cases examined were throat cultures from the immediate family of patients suffering from clinical diphtheria. In all, 202 cases were investigated, extending over a period of four months from April through July, 1906. The cultures were obtained through the courtesy of the medical inspectors of the Health Department, who took the cultures and forwarded them to us.

Park and Beebe's investigations of contact cases in 1894 showed 50 per cent of the throats infected with virulent Klebs-Löffler bacilli Of these 40 per cent subsequently developed diphtheria. These

TABLE 6.

CONTACT CASES. SEASON.

1906	Number Cases Examined	Total Diphtheria-like Bacilli in	Virulent Klebs-Löffler Bacilli in	Non-Virulent Diphtheria-like Bacilli	Pseudodiphtheria Bacilli (Hoffman's)	*B. xerosis*
April	148	13	11	2	19	
May	10	2	0	2	2	
June	2	0	0	0	2	
July	42	5	3	2	2	
Total	202	20	14	6	25	

TABLE 7.

CONTACT CASES. AGE.

Ages	Number Cases Examined	Total Diphtheria-like Bacilli Isolated from	Virulent Klebs-Löffler Bacilli in
Under 1 year	9	1	1
1–2 years	4	0	0
2–3 years	17	3	1
3–4 years	4	0	0
4–5 years	10	1	1
5–6 years	11	2	1
6–12 years	42	6	5
12–20 years	20	0	0
20+ years	65	6	5
Unknown	20	1	0
Total	202	20	14

persons all lived crowded together under the most unfavorable surroundings, often sleeping several in a bed with the infected patient. A second series of cultures from children living in more favorable conditions showed virulent bacilli in only 10 per cent. Kober found

virulent bacilli in 8.1 per cent of contacts, Hollstrom in 18.8 per cent, Aaser 20 per cent, Denny 11 per cent, Goadley 34.1 per cent (1900), Graham-Smith (1902) 10.4 per cent, etc. Thus the percentages vary according to conditions of environment, disinfection, etc.

From our 202 cases, organisms resembling diphtheria bacilli were isolated 20 times, 14 virulent and 6 non-virulent, that is, 7 per cent of the individuals were infected with virulent Klebs-Löffler bacilli. The subsequent history of these persons was not followed. The majority were older than those of the first series, more adults being included.

CONCLUSIONS.

1. Diphtheria-like organisms are present in a certain number of apparently normal throats, even where exposure to infection by diphtheria cannot be traced.

2. A certain proportion of these organisms (in our cases about one-third) are virulent, and the persons thus infected are a potential source of danger to the community while about two-thirds of the organisms are not true diphtheria bacilli and are probably harmless.

3. The other conditions being the same, virulent Klebs-Löffler bacilli are found in the mucous membranes of those exposed, about four times as often as in those apparently not exposed.

4. Mild sore throats and "colds" with bloody nasal discharge, such as are fairly common in children, should not be lightly considered. Whenever possible, cultures should be taken, and if diphtheria-like organisms are found, their virulence should be tested.

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